UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO

EXAMINER	
ART UNIT	PAPER NUMBER
	23

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 10-14-98.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-38 and 40-47 is/are pending in the application.

Of the above, claim(s) 14-18, 21, and ____ is/are withdrawn from consideration.

☐ Claim(s) ____ is/are allowed.

☒ Claim(s) 1-13, 19, 20, 23-38, and 40-47 is/are rejected.

☐ Claim(s) ____ is/are objected to.

☐ Claims ____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on ____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on ____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) ____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: ____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

✓ Notice of Reference Cited, PTO-892

✓ Information Disclosure Statement(s), PTO-1449, Paper No(s). 20

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

Serial Number: 08/948,393

Art Unit: 1623

The Group Art Unit assignment of this application is different from that of the parent application. To aid in association of papers with the file, it is requested that any future communications from Applicant reference Art Unit 1623.

The election of species requirement as first made in the Office action of 10-13-95, and later modified in the Office action of 03-05-96 in parent case 08/377,798, is maintained. Based on the first paragraph under Remarks of the response of 10-10-97, it is presumed that Applicant intends to continue prosecution of the previously elected species "carbohydrate" in the instant file wrapper continuation application. Thus, claims 1-13, 19, 20, 23-38, and 40-47 are treated herein, and claims 14-18, 21, and 22 are withdrawn from consideration.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 26-38, and 44-47 are rejected under 35 U.S.C. 112, first paragraph. In accordance with the reasoning of

In re Hyatt (218 USPQ 195 (CAFC 1983)), the instant claims cover every conceivable means for achieving the stated purpose(s). For example, claim 1 covers every conceivable means "for inhibiting interaction between P-selectin and a ligand of P-selectin and between E-selectin and a ligand of E-selectin". Therefore, the specification is not enabling for the entire scope of the claims because the specification discloses at most those means known to the inventor. Claims 1-12, 26-38, and 44-47 describe each agent solely in terms of its function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. See MPEP 2164.08(a).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13, 25, and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 13 is unclear as to the intended meanings of "a portion of said P-selectin" and of "a portion of said ligand of

P-selectin". The specification does not define what is meant by "portion",and the term has no art-recognized meaning in the instant context. Thus the metes and bounds of the claims cannot be determined.

Claim 25 is unclear as to the identity of the intended agent, specifically insofar as how it is to be "derived from" snake venom or a plant extract. It is noted that the specification does not described the intended derivation. Thus the metes and bounds of the claims cannot be determined.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the

inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13, 19, 20, 23-38, and 40-47 are rejected under 35 U.S.C. § 103 as being unpatentable over KOGAN *et al.* (A), RAO *et al.* (B), or SEEKAMP *et al.* (K), in view of ROSS (AF), further in view of JOHNSON-TIDEY *et al.* (K1).

Applicant claims a method of treating or preventing atherosclerosis in a mammal comprising administration of an agent which inhibits binding of P-selectin to a ligand. In accordance with the restriction requirement, the agent is a carbohydrate which does not contain peptide or protein moieties. The inhibitory agent may be a portion of P-selectin or a ligand thereof, including sialyl-Lewis x, sialyl-Lewis a, and their analogs.

Each of KOGAN, RAO, and SEEKAMP teaches oligosaccharides or their derivatives which may be used to block interaction of selectins with their ligands, and that such blocking is useful for treatment of certain cardiovascular disorders. See the Abstracts of KOGAN and SEEKAMP. See the Abstract and claim 1 of

RAO, as well as column 4, lines 12-23, and Figures 6-8. KOGAN and SEEKAMP further disclose that the oligosaccharides may be derivatives of sialyl-Lewis x or sialyl-Lewis a. KOGAN clarifies (Abstract, lines 1-3) that sialyl-Lewis x and sialyl-Lewis a are themselves ligands of P-selectin and E-selectin, and that they are found on cell surfaces. KOGAN further states that the oligosaccharide compounds are useful for inhibition of granular release, as in instant claim 26; see column 2, second full paragraph, for example. SEEKAMP and RAO also teach that the cell may be an endothelial cell, and that the ligand may be on a leukocyte such as a neutrophil; see SEEKAMP, first full paragraph, column 2, page 592, and RAO, column 8, lines 9-13). Each of the references indicates that the oligosaccharides disclosed inhibit the binding of molecules which are necessary for the function of P-selectin, as recited in claim 27. None of KOGAN, RAO, or SEEKAMP teaches that blocking the interaction of P-selectin or E-selectin with their ligands is useful specifically for treatment or prevention of atherosclerosis.

The ROSS reference is a review article which provides a thorough overview of the pathogenesis of atherosclerosis. ROSS confirms that the prior art had recognized the role of adhesion molecules such as selectins in atherogenesis. See, for example, the first full paragraph on page 805. The Examiner notes that ELAM is a selectin. ROSS also states that the adhesion molecules

may be on the surface of endothelial cells, and that the ligands may be on monocytes; see the first full paragraph on page 805. ROSS provides a description of the role of platelets in atherosclerosis, and suggests that inhibition of platelets is a means of treating atherosclerosis; see the first full paragraph on page 807. ROSS also describes the various stages of atherosclerosis as set forth in instant claims 28-36.

JOHNSON-TIDEY discloses that P-selectin and E-selectin are expressed in atherosclerotic lesions; see, for example, the abstract and page 952, right column, first full paragraph.

It would have been obvious for a person of ordinary skill in the art at the time of the invention to employ oligosaccharides such as derivatives of sialyl-Lewis x or sialyl-Lewis in a method of treatment or prevention of atherosclerosis, wherein the method is based on blocking the interaction of P-selectin and E-selectin with their ligands. The primary references had taught that such oligosaccharides could be used in treatment of highly related cardiovascular disorders by virtue of their inhibitory activity. This in itself would have motivated the ordinarily skilled artisan to treat atherosclerosis in a similar manner. The teaching of ROSS had specifically disclosed the link between atherosclerosis and cell adhesion molecules such as selectins, thereby providing one of ordinary skill in the art with a reasonable expectation of successful treatment of atherosclerosis

by this method. Given that the oligosaccharides of the primary references are taught to bind to P-selectin and E-selectin, it is not seen that the specific identity of the ligand, as in instant claim 7, provides for any patentable distinction. Furthermore, JOHNSON-TIDEY confirms that both P- and E-selectin are known to be involved with atherosclerosis. With regard to the specific dosage amounts of the newly added claims, no criticality has been demonstrated. These amounts are considered to be reasonably suggested by the references as applied.

Claims 1-12, 19, 20, 26-38, and 40-47 are rejected under 35 U.S.C. § 103 as being unpatentable over ROHRER *et al.* (L) in view of DE-AMBROSI (C), further in view of ROSS (AF), further in view of JOHNSON-TIDEY *et al.* (K1).

Applicant claims a method of treating or preventing atherosclerosis in a mammal comprising administration of an agent which inhibits binding of P-selectin and E-selectin to a ligand. In accordance with the restriction requirement, the agent is a carbohydrate which does not contain peptide or protein moieties. The inhibitory agent may be a portion of P-selectin or a ligand thereof, including heparin oligosaccharides.

ROHRER teaches that administration of heparin suppresses platelet granule secretion, and that this suppression occurs as a result of the ability of heparin to interfere with the

interaction between platelets and GMP-140; see the Abstract. The Examiner notes that GMP-140 is also known as P-selectin. ROHRER clearly states that platelet degranulation is implicated in atherogenesis (Abstract, lines 1-2). ROHRER also suggests that heparin fragments could be advantageously employed in place of standard heparin; see the final sentence of the Abstract. ROHRER does not explicitly disclose treatment or prevention of atherosclerosis by administration of heparin.

DE-AMBROSI teaches a method of treatment of thrombosis and atherosclerosis by administration of heparin derivatives (see claim 7 of the reference), further implies that other heparins would be expected to have similar therapeutic properties (see column 1, lines 21-30).

JOHNSON-TIDEY teaches as set forth above.

It would have been obvious for a person of ordinary skill in the art at the time of the invention to use heparin or its derivatives in a method of treatment or prevention of atherosclerosis, wherein the method requires inhibition of the interaction between P-selectin and its ligand. The ordinarily skilled worker would have been motivated to do so by ROHRER's disclosure that heparin could interfere in a process known to be associated with atherosclerosis, coupled with the teaching of DE-AMBROSI of a method of treatment of atherosclerosis based on administration of heparin derivatives. If further motivation is

needed, it is provided by ROSS's detailed description of the nature of the molecular interactions which lead to atherosclerosis. The comments set forth above with regard to ROSS also apply to the instant rejection. It is not seen that the specific identity of the ligand (instant claim 7), or the source from which the agent is derived (instant claim 25) provides for any patentable distinction. Furthermore, JOHNSON-TIDEY confirms that both P- and E-selectin are known to be involved with atherosclerosis. With regard to the specific dosage amounts of the newly added claims, no criticality has been demonstrated. These amounts are considered to be reasonably suggested by the references as applied.

Applicant's arguments filed 10-10-97 with regard to the art-based rejections, as well as the Wagner declaration, have been fully considered but they are not persuasive.

Applicant's argument, supported by the Wagner declaration, is that the state of the art at the time of the invention did not recognize the role of P-selectin in atherosclerosis. This argument is not convincing because it is contrary to art cited herein. Applicant will note that the rejections of the previous action have been modified to explicitly include the JOHNSON-TIDEY reference, which confirms the Examiner's position that the prior art had recognized the involvement of P- and E-selectin with

atherosclerosis. Also note the references cited below as additional prior art which further support the Examiner's position and tend to refute the claims of the Wagner declaration.

No claim is allowed.

Applicant is reminded that all references made of record in parent application 08/377,798 are of record in the instant file wrapper continuation application.

The following references are made of record to indicate the state of the art at the time of the invention more completely regarding the relationship between selectins and atherosclerosis: Gimbrone, Jr. (A1), see column 14, line 52 to column 15, line 6; McEver *et al.* (B1), see column 23, lines 31-48; Foulkes *et al.* (C1), see column 21, lines 7-54; and Ratcliffe (D1), see column 3, line 59 to column 4, line 47.

Papers relating to this application may be submitted to Technology Center 1600 by facsimile transmission. The number of the fax machine for official papers in Technology Center 1600 is (703) 308-4556. Any document submitted by facsimile transmission

will be considered an official communication unless the cover sheet clearly indicates that it is an informal communication.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Kathleen Kahler Fonda, at telephone number (703) 308-1620. Examiner Fonda can generally be reached from Tuesday through Friday, as well as on alternate Mondays, between 7:30 a.m. and 5:00 p.m. If the Examiner cannot be reached, questions may be addressed to Supervisory Patent Examiner John Kight, at (703) 308-0204. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

Kathleen Kahler Fonda, Ph.D.
Primary Examiner
Art Unit 1623